Remarks

Reconsideration of this Application is respectfully requested. Should the Examiner maintain any of the outstanding rejections, Applicants request an interview to further discuss the application.

Upon entry of the foregoing amendment, claims 90-114, 116-120 and 128-131 are pending in the application, with claims 90, 98, 106 and 114 being the independent claims. Claims 121, 124-127, 132, 133 and 136-140 were cancelled solely to expedite prosecution of the application and not in acquiescence to the Examiner's rejections. Support for the amendment to claim 106 can be found in the specification, for example, on page 7, lines 21-28 and in original claim 106. The above noted amendments are made solely to expedite prosecution and not in acquiescence to the Examiner's rejection. These changes and additions are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 101

The Office Action maintains the rejection of claims 90-114, 116-121, 124-133 and 136-140 under 35 U.S.C. § 101 for the reasons stated in the Office Action of PTO File Wrapper Paper No. 14. *See* PTO File Wrapper Paper No. 27, page 2, lines 9-12. However, Applicants traverse the rejection and continue to maintain that a *prima facie* case of non-utility has not been made. Moreover, Applicants have previously provided

post-filing date references which sufficiently demonstrate that the skilled artisan would find that the Specification describes a specific, substantial and credible utility for galectin 9. *See* Amendment and Reply Under 37 C.F.R. § 1.111, pp. 4-14, filed June 15, 2001, and exhibits cited therein; and Amendment and Reply Under 37 C.F.R. § 1.116, pp. 4-11, filed December 11, 2001, and exhibits cited therein. Here, Applicants provide additional post-filing date references which preclude a person having ordinary skill in the art from concluding that the Specification does not disclose a utility for galectin 9 which satisfies 35 U.S.C. §101.

Sato, M. *et al.*, "Functional analysis of the carbohydrate recognition domains and a linker peptide of galectin-9 as to eosinophil chemoattractant activity," *Glycobiology 12*: 191-197 (2002) (hereinafter, "Exhibit K") demonstrates the similar eosinophil chemoattractant (ECA) activity of three galectin 9 isoforms: galectin-9S, galectin-9M and galectin-9L. *See* Exhibit K, p. 193, especially Figure 4[1]. It is important to note that Applicants' galectin-9 is identical to galectin-9S. *See* NCBI Accession No. BAB83623, accessed on October 23, 2002, attached herewith as Exhibit L[2]. Therefore, Applicants' galectin 9 possesses ECA activity.

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[1] Galectin-9M is the same protein as ecalectin. *See* Exhibit K, p. 195, left column, lines 5-9. Hence, the terms "ecalectin" and "galectin-9" can be used interchangeably because they refer to the same protein.

[2] Exhibit L notes under "Features" that this 311 amino acid polypeptide is termed both "galectin 9" and "ecalectin short isoform." As noted *supra*, ecalectin is the same protein as galectin-9. *See* n. 1. It is also important to note the fact that Applicants' galectin 9 (or, galectin 9S) differs from galectin 9M only in that the latter contains a 12 amino acid insert (PPGVWPANPAPI). *See* Amendment and Reply Under 37 C.F.R. § 1.111, pp. 11-12, filed June 15, 2001 and Exhibit D cited therein.

Exhibit K also indicates that the consecutive, 12 amino acid-insert that is in the galectin-9M isoform and not present in Applicants' protein is in the linker region between the carbohydrate recognition domains. Exhibit K, p. 195, right hand column, third full paragraph. Exhibit K's authors state that this region is "not likely . . . [to] form an extended structure." *Id.* Moreover, Exhibit K explicitly states that "ECA activity does not depend on a specific structure of the linker peptide." *See Id.* at p. 191, last line of the Abstract. Thus, it is unlikely that the presence or omission of these 12 amino acids have any effect on either proteins' structure as they have no impact on the proteins' ECA activity.

In addition to describing galectin 9 activity, Exhibit K reiterates that this protein with its ECA activity is an important factor in both HD and the immune system. *See* Exhibit K, p. 191, right column, second paragraph under Introduction section, first sentence. Indeed, one of the same authors of Exhibit K previously concluded that "[d]ue to its ability to selectively attract eosinophils, ecalectin is an interesting target for the development of new therapeutic strategies designed to treat eosinophils-dependent pathological conditions." *See* Exhibit I, p. 8, Conclusion, previously submitted December 14, 2001. Asthma is prominently indicated as an exemplary pathological condition. *Id.* Thus, Exhibits K and I indicate that galectin 9 ECA activity is associated with asthma. Moreover, one of the authors of Exhibit K previously pointed out in his conclusion that "it is well known that patients with a particular form of HD . . . exhibit marked tissue eosinophilia." *See* Exhibit J, p. 9, Conclusion; previously submitted December 14, 2001. From this and other evidence of the relationship between HD and ECA-caused eosinophilia, this author concluded that "it is likely that Ecalectin also plays a role in the

pathogenesis of HD." *Id.* Thus, Exhibits K and J indicate that galectin 9's ECA activity is an important factor in HD.

The relationship between galectin 9 and asthma and HD is clearly identified in Applicants' Specification. In particular, Applicants assert that galectin 9 is useful for treating and diagnosing asthma and Hodgkin's disease (HD). *See* Specification, p. 27, line 20 to p. 31, line 11; especially p. 29, lines 3-9 and p. 30, lines 12-18. In therapeutic applications, galectin 9 can be used to raise antibodies which serve as antagonists to galectin 9 activity. *See Id.* at p. 31, lines 6-11. In diagnostic applications, galectin 9 can be used to raise antibodies to detect asthma and/or HD. *See Id.* at p. 29, lines 20-27. Moreover, Applicants have recognized epitopic regions of galectin 9. *See* Specification p. 5, lines 14-23; and p. 11 line 21 to p. 12 line 2. Deviations from normal galectin 9 activity are recognized by the Specification as manifesting in asthma and Hodgkin's disease. *Id.* at p. 30, lines 19-22. Hence, galectin 9 is useful for raising diagnostic and therapeutic antibodies for diagnosing or treating asthma and HD. These utilities are specific in that not all proteins are useful for raising antibodies to detect or treat asthma and/or HD. Moreover, these utilities are substantial in that diagnosis or treatment of asthma or HD represent real world utilities that would be immediately appreciated by the skilled artisan upon reading the disclosed specification. In view of Exhibits I, J, K and L, the skilled artisan would find Applicants' asserted utilities to be credible.

Applicants do not have to provide actual evidence of clinical success, contrary to the Examiner's implication. *See* MPEP § 2107.02 (I) at 2100-34. All that is required of Applicants is that there be a *reasonable* correlation between the biological activity and the asserted utility. *See Nelson v. Bowler*, 626 F.2d at 857.

In addition, Exhibit K confirms that lactose binding activity, as recognized by Applicants' Specification at p.16, lines 21-24, is important to galectin 9's biological activity. In particular, Exhibit K indicates that the immune-modulatory effects of galectin 9 can be understood by "elucidat[ing] the function of each CRD [carbohydrate recognition domain] in relation to its carbohydrate binding specificity." *See* Exhibit K, p. 191, right column, second paragraph under Introduction section, last sentence. Moreover, the authors state that galectin 9's carbohydrate binding plays an important role in its ECA activity. *Id.* at p. 192, left column, lines 2-4. Finally, the authors indicate that the "ECA activity of galectin-9 is inhibited by lactose and mutated CRDs lacking carbohydrate binding activity lose ECA activity, showing that the interaction between the two CRDs of galectin-9 and cell surface glycoconjugate(s) is an essential step in eosinophil chemoattraction." *Id.* at p. 195, left column, lines 15-19.

Hence, the ability of galectin 9 to bind lactose is an indicator of its ECA activity. Applicants recognized that "galectin . . . 9 . . . protein activity can be measured using a lactose binding assay." *See* Specification, p. 16, lines 19-20. Hence, the Specification recognized both the lactose binding activity of galectin 9 and clinical manifestations associated with deviations in that activity. Given the above discussion, the skilled artisan would find that Applicants' Specification recognized a specific, substantial and credible use of galectin 9.

In view of the facts set out above, Applicants submit that the skilled artisan would not reasonably doubt that their galectin 9 is useful, *inter alia*, for therapeutic treatment of certain immunomodulatory disorders. For example, galectin 9 can be used to create antibodies or screen for other antagonists which can be used in therapeutic

regimens for individuals suffering from elevated levels of galectin 9 associated activity[3]. Such uses of galectin 9 are specific to galectin 9 associated disorders and substantial in that diagnosis or treatment are immediately appreciated real world utilities. Moreover, as discussed *supra* and in the previously filed responses, Applicants' specification recognized a diagnostic utility for detection of the disorders associated with galectin 9 activity. As such, Applicants assert that the presently claimed invention possesses a specific, substantial and credible utility that constitutes a patentable utility under 35 U.S.C. § 101. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112

The Examiner has rejected claims 90, 92, 94-98, 100 and 102-114, 116-120, 128-131, 133 and 136-140 under 35 U.S.C. § 112. File Wrapper Paper No. 27, page 10. In particular, the Examiner alleges that the written description does not enable these claims.

Solely to expedite prosecution and not in acquiescence to the Examiner's rejection, Applicants have cancelled claims 121, 133 and their respective dependent claims. Solely to expedite prosecution and not in acquiescence to the Examiner's rejection, Applicants have amended independent claims 106 and 114 with the term "consisting." It is believed that these amendments render the enablement rejections of these claims under 35 U.S.C. § 112 moot.

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[3] It is noted that an increase in galectin 9 associated ECA activity induces eosinophilia. *See* Exhibit E, p. 8355, left column, first paragraph below Abstract, previously filed on June 15, 2001.

With respect to claims 90, 98 and their respective dependent claims, it is reiterated that these claims are directed to proteins having lactose binding activity. In light of Exhibit K provided herewith, and the important role lactose binding plays in galectin 9 activity, Applicants assert that the specification enables the skilled artisan to practice the full scope of the claims. The skilled artisan will understand that modifications that prevent galectin 9 from binding lactose are outside of the scope of the claims. Moreover, the Specification provides the skilled artisan with the techniques needed to assess lactose binding. *See* Specification, p. 16, line 21 to p. 17, line 14.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the § 112 rejection of claims 90, 92, 94-98, 100 and 102-114, 116-120, and 128-131.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 121, 124, 125 and 132 under 35 U.S.C. § 102(b) as being anticipated by Oda *et al.* as evidenced by Accession Number A46631. *See* PTO File Wrapper Paper No. 27, page 15, lines 9-11. The Examiner has also rejected claims 121, 124-126 and 132 under 35 U.S.C. § 102(b) as being anticipated by Mehul *et al.* as evidenced by Accession Number A54909. *Id.* at page 16, lines 3-5. Furthermore, the Examiner has rejected claims 121, 127 and 132 under 35 U.S.C. § 102(b) as being anticipated by Foddy *et al.* as evidenced by Mehul *et al.* and Accession Number A54909. *See* PTO File Wrapper Paper No. 27, page 16, lines 20-23.

Solely to expedite prosecution of the application and not in acquiescence to the §102 rejections, Applicants have cancelled claim 121 and its dependent claims. Accordingly, it is believed that the above noted rejections under §102(b) are now moot.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Version with markings to show changes made

Claim 106. (twice amended) An isolated protein comprising [an amino acid sequence selected from the group consisting of:] a fragment of the amino acid sequence of SEQ ID NO:4;

wherein said fragment consists of an amino acid sequence selected from the group consisting of:

(a) amino acids 62 to 102 in SEQ ID NO:4;
(b) amino acids 226 to 259 in SEQ ID NO:4; and
(c) amino acids 197 to 308 in SEQ ID NO:4[;

wherein said protein has lactose binding activity].

Claim 114. (thrice amended) An isolated protein [comprising] consisting of at least 30 contiguous amino acids of SEQ ID NO:4[, wherein said protein has lactose binding activity].

Claims 121, 124-127, 132, 133 and 136-140 were cancelled.